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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/779,369	02/13/2004	Robert J. Hariri	9516-141-999	2020

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EXAMINER	
BARNHART, LORA ELIZABETH	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/779,369	**Applicant(s)** HARIRI, ROBERT J.	
	Examiner Lora E. Barnhart	**Art Unit** 1651	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 23 May 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *05 May 2006*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-11,13-18 and 21-28*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: Please see attached sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

SANDRA E. SAUCIER
PRIMARY EXAMINER

Reply to Request for Reconsideration

Claims 1-11, 13-18, and 21-28 stand rejected under 35 U.S.C. § 103(a) as being obvious over Boyse et al. (1991, U.S. Patent 5,004,681) taken in view of Kondo (1998, *Clin Exp Allergy* 28: 1340-1344), Sakabe et al. (1997, *Stem Cells* 13:73-81), Gluckman et al. (1998, *Hematology* pages 1-14), and Gluckman et al. (2001, *Transfus. Clin. Biol.* 8:146-154) for reasons of record.

Applicant alleges that Gluckman (1998), while suggesting the administration of "a high number" of nucleated cord blood cells, does not suggest numbers as high as those instantly claimed (Remarks, page 4, paragraph 5). In particular, applicant alleges that Gluckman (1998) teaches that "the most nucleated cells obtained from a single unit of cord blood was $58x10^{8}$" and that Gluckman (1998) does not suggest administering more than one single unit of cord blood (Remarks, page 5, paragraph 1). Applicant further alleges that Gluckman (1998) "merely suggests pooling as an 'avenue of research'" (Remarks, page 5, paragraph 2). Applicant urges that Gluckman (2001) teaches that administering unmatched cord blood to recipients causes graft-versus-host disease (GVHD) in 21% of patients (Remarks, page 5, paragraph 3). Applicant alleges that the prior art does not teach the treatment of the conditions recited in claims 10 and 14-18, citing *Perricone v. Medicis Pharmaceutical Corp.*, 77 USPQ2d 1321 (CA FC 2005) (Remarks, page 7, paragraph 3). These arguments have been fully considered, but they are not persuasive.

It is a well-held tenet of patent law that in general, differences in concentration or temperature will not support the patentability of subject matter encompassed by the

prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955), and M.P.E.P. § 2144.05 (II). Applicant appears to be alleging that the claimed numbers of administered cells are critical to the success of the treatment method; however, this allegation is insufficient to demonstrate patentability of the claimed numbers. To establish unexpected results over a claimed range, applicants should compare a sufficient number of tests both inside and outside the claimed range to show the criticality of the claimed range. *In re Hill*, 284 F.2d 955, 128 USPQ 197 (CCPA 1960), and M.P.E.P. § 716.02 (d) (II). Applicant has provided no substantive evidence that the numbers of cells in the instant claims are critical to the patentability of the claimed method. Without such a showing, the instantly claimed numbers of cells cannot be considered inventive.

Whether Gluckman (1998) exemplified pooling of samples is immaterial to the obviousness of pooling samples. A single unit of cord blood is taught by Boyse et al., Gluckman (1998), and Gluckman (2001) to be useful in treating various conditions; combining one unit with another equates to combining two compositions with usefulness for a particular purpose for that same purpose. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Again,

absent a substantive evidentiary showing that administering more than one unit of cord blood yields unexpected results, administering more than one unit (as suggested by applicant at page 6, lines 17-19, of the as-filed specification) is not inventive.

Applicant refers to page 153, column 1, paragraph 3, lines 12-14, of Gluckman (2001) in support of his contention that the person of ordinary skill in the art would not have been motivated to administer mismatched cord blood to patients because 21% of patients develop grade II-IV GVHD. However, this paragraph also points out that 73% of patients administered HLA-matched bone marrow develop grade II-IV GVHD (lines 5-12). Therefore, the person of ordinary skill in the art would have been motivated at the time the invention was made to replace matched bone marrow transplants with mismatched cord blood transplants, since the incidence of grade II-IV GVHD is more than three times less likely with the latter.

Applicant urges that Boyse et al. does not suggest treatment of all of the conditions recited in claims 10 and 14-18 as claimed. However, Boyse et al. is not applied alone, but in combination with various secondary references, and the claimed invention becomes obvious when the references are considered together as a whole rather than each alone. Applicant cites *Perricone v. Medicis Pharmaceutical Corp.* in support of his arguments, but the examiner points out that the fact pattern in *Perricone* does not match the pattern in the instant case; in *Perricone*, there was no pending obviousness rejection, as there is in this case.

Applicant is invited to provide substantive evidence that the claimed numbers of cells are inventive. Evidence of unexpected properties may be in the form of a direct or

indirect comparison of the claimed invention with the closest prior art that is commensurate in scope with the claims. See *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980) and M.P.E.P. § 716.02(d) - § 716.02(e). See *In re Blondel*, 499 F.2d 1311, 1317, 182 USPQ 294, 298 (CCPA 1974) and *In re Fouche*, 439 F.2d 1237, 1241-42, 169 USPQ 429, 433 (CCPA 1971) for examples of cases where indirect comparative testing was found sufficient to rebut a prima facie case of obviousness. The nonobviousness of a broader claimed range can be supported by evidence based on unexpected results from testing a narrower range if one of ordinary skill in the art would be able to determine a trend in the exemplified data which would allow the artisan to reasonably extend the probative value thereof. *In re Kollman*, 595 F.2d 48, 201 USPQ 193 (CCPA 1979). Applicant is urged to provide a declaration comprising evidence of, for example, unexpected results for the claimed range of number of administered cells. "The reason for requiring evidence in declaration or affidavit form is to obtain the assurances that any statements or representations made are correct, as provided by 35 U.S.C. § 25 and 18 U.S.C. § 1001." Permitting a publication to substitute for expert testimony would circumvent the guarantees built into the statute. *Ex parte Gray*, 10 USPQ2d 1922, 1928 (Bd. Pat. App. & Inter. 1989). Publications may, however, be evidence of the facts in issue and should be considered to the extent that they are probative. M.P.E.P. § 716.02 (g).

SANDRA E. SAUCIER
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